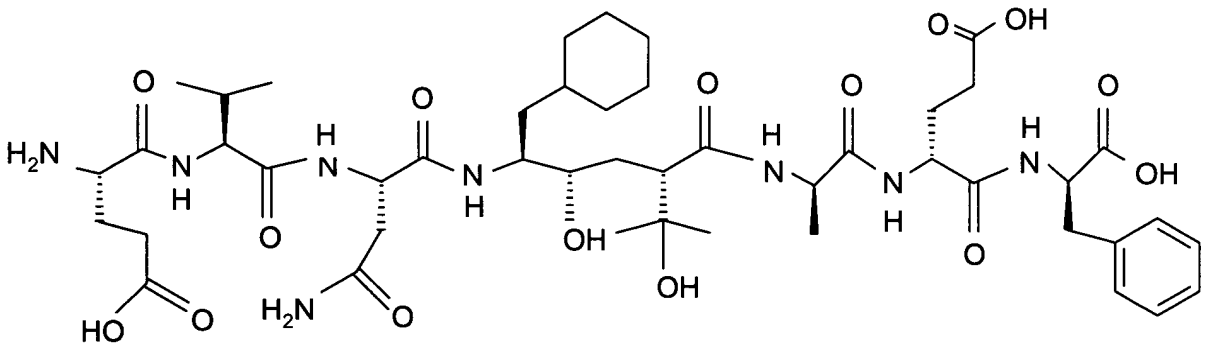
REMARKS

The Office Action has rejected Claims 1-15 under 35 U.S.C. §112, first paragraph, as allegedly being non-enabling.

In response, applicants submit the following Remarks, which are deemed to place the present case in condition for allowance. Favorable consideration is respectfully requested.

The present invention is directed, inter alia, to a compound of the formula



or its pharmaceutically acceptable salts, a pharmaceutical composition containing same and a method of treating various neurological disorders, such as Alzheimer's disease, , Crutzfield-Jacob's disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stroke, Down's syndrome, pancreatitis, inclusion body myocitis, other peripheral amyloidoses and diabetes.

Pursuant to the rejection of Claims 1-15 under 35 U.S.C. §112, first paragraph, the Office Action alleges that it does not believe that the above-identified compound or its pharmaceutically acceptable salt will be useful for treating the various diseases listed hereinabove. In evaluating the enablement issues, the Office Action considers various factors that have been used to determine whether a disclosure meets the enablement requirement, such as (1) the nature of the invention, (2) the state of the prior art, (3) the level of ordinary

skill in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. These factors are listed in In re Wands, 858 F2d. 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

It is to be noted that it is improper to conclude that a disclosure is not enabling based on the analysis of only one of the factors. Id. Further, the analysis by the United States Patent and Trademark Office must consider all of the evidence related to each of these factors and any conclusion of non-enablement must be based on the evidence as a whole. Id., 858 F2d. at 737, 8 USPQ2d at 1404. The conclusion of enablement or non-enablement is reached by weighing all of the above noted factual considerations. Id., 858 F2d. at 737, 8 USPQ2d at 1404.

According to the Office Action, the application is deficient in each of the categories and it concludes that the instant application does not enable the claimed invention.

Hereinbelow, applicants will analyze each of these factors listed hereinabove and show that the United States Patent and Trademark Office has not met out a prima facie case of non-enablement and that the present application is enabling, in compliance with the requirements of 35 U.S.C. §112, first paragraph.

With respect to the first factor, the present invention is directed to one compound and its pharmaceutically acceptable salts and a pharmaceutical composition containing same and the use thereof for treating various diseases listed in Claim 3. Thus, the claimed invention is relatively narrow.

In discussing the second factor, the Office Action admits that the prior art of record does not teach or suggest a compound having a structure the same or similar to that

specified in Claim 1. Moreover, the above compound is an inhibitor of beta amyloid cleavage enzyme (BACE).

Nevertheless, there is relevant prior art that needs to be taken into account when evaluating this factor. At the time of the filing of the above-identified application, it was known that a number of important neurological diseases, including Alzheimer's disease, cerebral amyloid angiopathy and prion mediated disease are characterized by the deposition of aggregated proteins, referred to as amyloid, in the central nervous system. Both Alzheimer's disease and cerebral amyloid angiopathy are characterized by the accumulation of senile plaques in the brains of the affected individuals. The main amyloid component is amyloid beta protein. In fact, it was generally accepted at the time of the filing of the above-identified application that the accumulation of beta-amyloid peptides in human brain is a major cause of Alzheimer's disease. See WO 01/00665, pg. 4, Hong, et al., Science, 2000, 290, 150. The Beta-amyloid cleavage enzyme (BACE) is a key protease involved in the production in human brain of beta amyloid peptide from beta-amyloid precursor protein. WO 01/00665; pg. 4; Hong, et al., Science 2000, 290, 150. Thus, it was generally believed that inhibitors specifically designed for BACE were believed to inhibit or decrease the formation of beta amyloid peptides and the progression of Alzheimer's disease. WO 01/0665; p. 4; Hong, et al., Science 2000, 290, 150.

In its analysis, the Office Action refers to WO patent application No. 01/00665, wherein it stated that at the time of the filing of its underlying application there is no effective palliative or preventive drug for treating Alzheimer's disease. However, WO 01/00665 was filed prior to the filing of the present application; thus, the compound recited in Claim 1 was unknown to the public at the time. Such statement, therefore does not have any

bearing on the utility of the claimed compounds. The same comments are also applicable with respect to the Potter reference, referred to by the Office Action as it was published prior to the filing of the above-identified application.

With respect to item three of the factors, the Office Action alleges that the relative skill in the art is high; but it does not qualify it. High is quite ambiguous. Does it mean that the person of ordinary skill in the art has a Ph.D.?

The Office Action alleges in item (4) that the art is not able to predict whether a compound can be used to treat the diseases mentioned in the absence of experimental testing. It refers to the Potter article, which questions whether the discovery of the β-secretatase provides a clear target for Alzheimer's drug development. However, Potter provides no scientific evidence in support of its allegation; it is purely speculative. Moreover, this speculation is contrary to the general beliefs of scientists at the time. (See, discussions of Factor 2), i.e., it was generally believed that inhibitors specifically designed for BACE were believed to inhibit or decrease the formation of beta amyloid peptides and the progression of Alzheimer's disease.

With respect to item 5, the Office Acton alleges that the claims are relatively broad.

Applicants respectfully submit that the claims are relatively narrow. They are directed to the use of one compound or a pharmaceutically acceptable salt thereof. Contrary to the allegations in the Office Action, the subject matter in the claims is not broad.

The Office Action alleges, without any reference to any paper or publication or other evidence, "that the diseases alleged to be treated with the exception of Alzheimer's

disease are not caused by the enzyme which is to be inhibited by the claimed compound". Page 3 of Office Action.

However, with respect to the non-enablement requirement, the burden is on the United States Patent and Trademark Office to establish that the claimed subject matter is not enabled. Case law has held that a specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Marzocchi, 439 F2d. 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the Court, "it is incumbent upon the Patent Office, wherever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicants to go to the trouble and expense of supporting his presumptively accurate disclosures". Id.

The Office Action acknowledges that BACE is a cause of Alzheimer's disease. As described hereinabove in the discussion of Factor 1, the contents of which are incorporated by reference, it was generally believed at the time of the filing of the underlying application that a compound that inhibits BACE would be useful for treating various neurological diseases, including Alzheimer's disease. As described in the application and shown on Page 10, lines 15-22 of the instant specification, the compound of the present invention, using standard assays known to one of ordinary skill in the art, binds to the BACE enzyme with IC_{50}

value equal to $49x10^{-9}$ M, thereby providing evidence that it inhibits the same. Accordingly, based upon the teachings in the present application, one skilled in the art, reading the present disclosure, would believe that the compound or pharmaceutically acceptable salt of the present invention would be useful for treating Alzheimer's disease.

With respect to the use of the compound or pharmaceutically acceptable salt thereof, as held by the Marzocchi Court, the Office Action must accept as true the assertions of the present utility, unless there is evidence to the contrary. However, the Office Action provided no evidence which shows that the compound or the pharmaceutically acceptable salt thereof do not have the requisite utility. It did not refer to any article or publication which demonstrates that the compounds of the present invention do not work. It provided no evidence whatsoever. Thus, in the absence of evidence to the contrary, in accordance with the holding In re Marzocchi, the utility of the compound of the present invention must be accepted as true. The only disease, which the Office Action tried to provide evidence that the claimed compound or its pharmaceutically acceptable salts is not enabled in the present application for treating Alzheimer's disease, but as indicated hereinabove, the Office Action has not met its burden.

The Office Action alleges that there are no working examples, but case law has held that working examples are not necessary if the invention is otherwise disclosed in such a manner that one of ordinary skill in the art is able to practice it without an undue amount of experimentation. In re Borkowski, 422 F2d. 904, 908, 164 USPQ 644, 645 (CCPA 1970). Here the application is enabling. It teaches one of ordinary skill in the art how to make and use the compounds. The process for preparing the compound is described on Page 6, line 1 to Page 10, line 14 and Examples 1-2 on pages 12-15 of the instant specification. It teaches one

of ordinary skill in the art how to use the present compound and its pharmaceutically acceptable salts. Attention is directed to Page 10, line 14 to Page 12, line 15 and Page 4, lines 17 to Page 5, line 14 of the instant specification. The specification also provides the preferred amount to be administered as well as the various modes of administration. Thus, the instant specification provides the preparation of a pharmaceutical composition, the method of administration and the method of treating various diseases in a manner sufficient for one of ordinary skill in the art to make and practice the invention without an undue amount of experimentation.

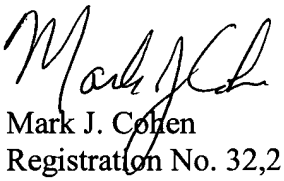
Thus, contrary to the allegations in the Office Action, the present invention can be practiced without an undue amount of experimentation.

When weighing the factors listed hereinabove, there can be only one conclusion reached regarding enablement. Contrary to the allegations in the Office Action, the Office Action has not made out a prima facie case of non-enablement, even though it has the burden on such issue. Moreover, the instant specification provides an enabling disclosure commensurate in scope with the claimed invention without an undue amount of experimentation.

Thus, for the reasons given herein, the rejection of Claims 1-15 under 35 U.S.C. §112, first paragraph is obviated; withdrawal thereof is respectfully requested.

Thus, in view of the Remarks hereinabove, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Mark J. Cohen
Registration No. 32,211

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, New York 11530
(516) 742-4343

MJC:lf